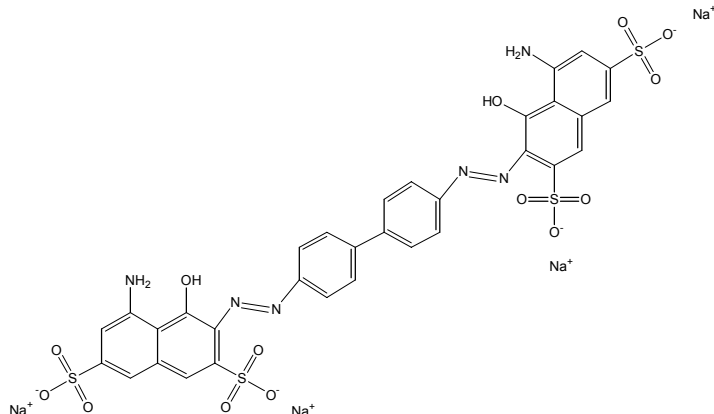


DIRECT BLUE 6 CAS No. 2602-46-2

First Listed in the *Third Annual Report on Carcinogens* as *Reasonably Anticipated to be a Human Carcinogen*, updated to *Known to be a Human Carcinogen* in the *Ninth Report on Carcinogens*



CARCINOGENICITY

Direct Blue 6 is *known to be a human carcinogen* based on the listing of benzidine-based dyes that are metabolized to benzidine as *known to be human carcinogens* in the Report on Carcinogens (NTP, 2000). This listing is based on the following observations: 1) benzidine is a known human carcinogen (IARC V.1, 1972; IARC, S.1, 1979; V.29, 1982; IARC S.7, 1987; and NTP, 1998); 2) metabolism of benzidine-based dyes, including Direct Blue 6, to release free benzidine is a generalized phenomenon in humans and all experimental animal species studied, (Rinde and Troll, 1975; Lynn et al., 1980; Nony and Bowman, 1980; Lowry et al., 1980; and Martin and Kennelly, 1985); 3) benzidine exposure from exposure to benzidine-based dyes is equivalent to exposure to equimolar doses of benzidine (Lynn et al., 1980); and 4) all available evidence indicates benzidine-based dyes are animal carcinogens and represent a carcinogenic risk to humans (NCI 108, 1978; IARC, V.29, 1982; IARC S.4, 1982). There are no epidemiology studies available to assess the human carcinogenicity of Direct Blue 6 alone.

There is sufficient evidence for the carcinogenicity of Direct Blue 6 (technical grade) in experimental animals. In a single study, administration of technical-grade Direct Blue 6 in the diet induced liver hepatocellular carcinomas and neoplastic nodules in rats of both sexes. There is no evidence that technical grade Direct Blue 6 was carcinogenic to mice under the same conditions (IARC V.29, 1982; IARC S.4, 1982; IARC S.7, 1987).

PROPERTIES

Direct Blue 6 occurs as a blue-violet solid. It is soluble in water, slightly soluble in ethanol and ethylene glycol monoethyl ether, and insoluble in other organic solvents. When heated to decomposition, Direct Blue 6 emits toxic fumes of nitrogen oxides (NO_x) and sulfur oxides (SO_x). The benzidine content of domestically produced Direct Blue 6 has been measured as being between 4 and 12 mg/kg. The composition of commercial Direct Blue 6 varies in order to meet individual shade and intensity requirements.

USE

Direct Blue 6 is possibly used to dye fabric, leather, silk, wool, cotton, cellulosic materials, and paper, to stain biological materials, and to produce aqueous inks (IARC V.29, 1982; NIOSH 24, 1978). CPSC and EPA indicated that artists also may use the chemical. Direct Blue 6 has been used as a hair dye component, but FDA indicated that it presently is not used by the cosmetic industry (NIOSH 24, 1978).

PRODUCTION

There is currently one U.S. manufacturer of Direct Blue 6 (HSDB, 1998). No suppliers of the compound, however, were named in *Chemyclopedia 98* and the 1998 *Chemical Buyers Directory* (Rodnan, 1997; Tilton, 1997). In 1990 Chem Sources identified two suppliers of Direct Blue 6 (Chem Sources, 1991). The USITC identified one producer of Direct Blue 6 in 1979 and 1982, with implied annual production volumes of > 5,000 lb (USITC, 1983). In 1978, domestic companies produced nearly 62,000 lb of Direct Blue 6 and imported 4,400 lb (IARC V.29, 1982; NIOSH Review, 1980). The 1979 TSCA Inventory identified three companies producing 110,500 lb and two companies importing 5,500 lb in 1977. The CBI Aggregate was less than 1 million lb (TSCA, 1979). No data on exports of Direct Blue 6 were available. Direct Blue 6 was first produced in commercial quantities in the U.S. in 1914 (IARC V.29, 1982).

EXPOSURE

The primary routes of potential human exposure to Direct Blue 6 are inhalation, ingestion, and dermal contact. According to CPSC, the use of benzidine congener dyes in consumer dyeing products and commercial textile applications has been voluntarily decreased. The primary source for potential exposure to Direct Blue 6 is at the production site. The initial production step is in a closed system, but other production operations (e.g., filtering, drying, and blending) may be performed in the open and therefore may afford greater potential for worker exposure. The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 1,300 workers were possibly exposed to Direct Blue 6 (NIOSH, 1976). In 1980, NIOSH estimated that about 500 workers were potentially exposed to the dye in the workplace (NIOSH Review, 1980). Occupational exposure to Direct Blue 6 may occur for workers in a variety of industries identified by NIOSH, including paper and allied products, petroleum and related industries, rubber and plastic products, leather and leather products, instrumentation and measuring devices, and banking. In addition, the textile industry accounts for substantial risk for occupational exposure. Direct Blue 6 has been detected in the workplace air of a textile dyeing operation, at total airborne particulate concentrations of 1.20-3.94 mg/m³. It has been estimated that 25% of the benzidine-derived azo dyes are applied to textiles, 40% to paper, 15% to leather, and the remainder to other diverse applications (NIOSH 24, 1978; IARC V.29, 1982).

The general population may possibly be exposed to Direct Blue 6 through the use of retail packaged dyes containing the benzidine-based dye. Potential consumer exposure to Direct Blue 6 depends upon the ability of the dye to migrate out of the consumer product and either penetrate the skin or break down prior to penetrating the skin. A risk of potential exposure to Direct Blue 6 may have existed for people using hair dyes which contained the compound. In addition, ingestion of Direct Blue 6 may occur if food is eaten which contained residues from packaging in which the dye was used.

REGULATIONS

In late 1980, CPSC collected scientific and economic data to propose a ban on the use of all benzidine congener dyes in consumer products. CPSC also completed studies on the dermal penetration of two of these dyes, and noted no dermal penetration. The use of benzidine congener dyes in retail packaged dyes for home and school use has been voluntarily decreased. Therefore, CPSC voted to deny the petition that requested a ban of these consumer dye products. Educational materials have been developed and are available to warn artists of the potential danger of benzidine congener dyes. EPA regulates Direct Blue 6 under the Superfund Amendments and Reauthorization Act (SARA), and the Toxic Substances Control Act (TSCA), subjecting it to reporting requirements. FDA does not regulate the cosmetic use of Direct Blue 6, but was petitioned to approve the chemical for use as an indirect food additive (e.g., as a dye for paper and paperboard products). In 1979, the petition was withdrawn. OSHA regulates Direct Blue 6 under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table A-24.